REMARKS

Claims 2, 5-8, 16-18, 35, 37, and 39-41 will be pending after the entry of the amendment with this response. Claims 1, 11, 12, 19, 22, 25, 26, 33, 34, 36, and 38 have been previously canceled without prejudice in the interest of advancing prosecution.

Objections to Claims

The Examiner maintained but has held in abeyance the objections to claims 8 and 16-17 for not being limited to the elected species.

Applicants respectfully traverse the objection to claim 5 as not narrowing claim 2. As a preliminary matter, Applicants amended claim 5 so that there is a proper antecedent to claim 2. The recitation of endogenous morphogen in claim 2 is a part of characterization of the recited components. In other words, there may possibly be a monoclonal antibody to a gp130 protein which does not reduce inhibition of growth-promoting effects of endogenous morphogens *in vitro*, and use of such antibody is not within the scope of what Applicants claim as their invention. In contrast, claim 5 recites an endogenous morphogen as an agent that is present in the cells subject to this method, the release of the inhibition of which causes dendritic growth. Therefore, claim 2 can be practiced in a situation where an exogenous or endogenous morphogen is the target of the release of the inhibition, whereas claim 5 covers only the endogenous morphogen. In other words, to practice the invention of claim 5, one need not add exogenous morphogen but enhance the activity of existing morphogen to promote the neuronal growth. This is complemented by claim 6, where an exogenous morphogen is recited.

35 USC §112, first paragraph

The examiner maintained rejection of claims 2, 5-8, 16-18, 35, 37 and 39, alleging these claims are not enabled by the disclosure of the specification for the full scope of the claims. The Examiner states that the specification does not provide sufficient guidance to enable a skilled artisan to understand and carry out the invention *in vivo*.

The Examiner rejects the pending claims as not enabled, alleging insufficient disclosure for in vivo administration. The claims relate generally to methods of promoting dendritic growth. At the time the application was filed, components of the composition described in the pending claims have been used *in vivo* in experimental animals, albeit for purposes other than reducing the inhibition of morphogen induced dendrite growth. One skilled in the art would know generally the concentration range of a monoclonal antibody to administer to a mammal. The use of cyclic AMP antagonists recited herein and their characteristics were generally known as well. Applicants submit that it would have been within the knowledge of one skilled in the art at the time to practice the method to promote dendritic growth, and such skilled artisan did not need further guidance.

The Examiner is also concerned that *in vivo* results are not predictable by the *in vitro* data because *in vitro* experiments are carried out with only sympathetic neuronal culture, whereas there are other cell types *in vivo*.

Applicants submit that the *in vitro* systems used by Applicants reflect *in vivo* utility of a composition. In publications after the application was filed, the utility of morphogens *in vivo* has been documented. For instance, Chang *et al.*, Stroke, 2003,34: 558-564, reported that when BMP-7 was administered systemically to rats one day after they were inflicted with experimental occlusion to induce ischemia, a well-accepted model for stroke, the experimental animals' locomotor activity increased in a statistically significant way. This result indicates a morphogen is effective *in vivo* to improve damages to neurons due to stroke, which is one of the examples of the cause of injury claimed in the instant application. The authors of the referenced article also state that they have data indicating MBP-7 can elicit new neurite outgrowth. In addition, Applicants and colleagues were granted a United States Patent No. 6,723,698, the claims of which relate to treatment of mammals inflicted with amylotrophic lateral sclerosis or spinal cord injury, and a United States Patent No. 6,506,729 for the treatment of Parkinson's disease, by administering a morphogen. Enhancing morphogen activity to elicit neuronal dendritic growth is reasonably expected to be similar to increasing morphogen activity by administering a morphogen itself.

In addition, the Examiner asserts neurons injured by neurodegenerative diseases, including stroke, recited in claim 8 are dead or dying. Applicants believe it is unnecessary to point out that the neurons subject to this invention are alive. With regard to the neurons that are "dying," Applicants have not use the word in the claim for its indefinite nature – in its broadest sense, any non-immortalized and/or non-stem cell can be said to be dying at any given time. On the other hand, an injured cell is a cell that has sustained damages that are not a part of the natural cell cycle or natural status of the cell. It may still be repaired. As such, Applicants respectfully disagree with the Examiner's conclusion that because a cell is injured by a neurodegenerative disease, such cell would not recover.

With regard to cell types, according to a review by Chen and Panchision, Stem Cells 2007, 25: 63-68, it has been reported that neurons from cortical, hippocampal, striatal, and mid-brain dopaminergic neurons as well as PNS superior cervical ganglion. (See page 66, left column.) Applicants submit that the effect of morphogen is not limited to sympathetic neurons.

With regard to the Examiner's rejection of claims 39-41, Applicants respectfully submit that the Examiner's data interpretation is incorrect. In Figure 5, the control samples that did not receive LIF still showed some trend that, when LIF antibody was added to the sample, the number of dendrites were more numerous than with no LIF antibody. However, in the interest of advancing prosecution of the instant application, Applicants amended to recite the presence of a morphogen and an inhibiting condition.

Applicants submit that the amended claims are supported by the specification, and respectfully request that the rejection on this ground be withdrawn.

35 USC §112, second paragraph

Claims 5-6, 39 and 40 are rejected as allegedly being indefinite for reciting "morphogen activity." Claims 5 and 6 have been amended and no longer recite "morphogen activity." Claims 39 and 40 were amended to specifically recite inducing dendrite growth as the morphogen activity. Applicants respectfully request that the rejection on this ground be withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Applicant believes no additional fee is due with this response. However, if an additional fee is due, please charge our Deposit Account No. 18-1945, under Order No. JJJ-P01-569 from which the undersigned is authorized to draw.

Dated: May 1, 2007

Respectfully submitted,

By _____

Erika Takeuchi
Registration No.: 55,661
FISH & NEAVE IP GROUP,
ROPES & GRAY LLP
1211 Avenue of the Americas
New York, New York 10036
(212) 596-9000
(212) 596-9090 (Fax)
Attorneys/Agents For Applicant